



H.A.

0300
PATENT
#5

Attorney Docket No. NIH-05065

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Lawrence E. Samelson *et al.*

Serial No.: 09/597,920

Group No.:

Filed: 06/19/00

Examiner:

Entitled: **THE PROTEIN TYROSINE KINASE SUBSTRATE
LAT AND ITS USE IN THE IDENTIFICATION OF
(ANT)AGONISTS OF THE KINASE**

**INFORMATION DISCLOSURE
STATEMENT TRANSMITTAL**

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: May 25, 2001

By: Marilyn Moy

Marilyn Moy

Sir or Madam:

Enclosed please find an Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. 08-1290. An originally executed duplicate of this transmittal is enclosed for this purpose.

Dated: May 25, 2001

Kamrin T. MacKnight
Kamrin T. MacKnight
Registration No. 38,230

MEDLEN & CARROLL, LLP
220 Montgomery Street, Suite 2200
San Francisco, California 94104
415/705-8410



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor Application of: Lawrence E. Samelson *et al.*

Serial No.: not yet assigned

Group No.:

Filed: 06/19/00

Examiner:

Entitled: **THE PROTEIN TYROSINE KINASE
SUBSTRATE LAT AND ITS USE IN THE
IDENTIFICATION OF (ANT)AGONISTS OF
THE KINASE**

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

<p align="center">CERTIFICATE OF MAILING UNDER 37 CFR § 1.8(a)</p> <p>I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231 on May 25, 2001.</p> <p>By: <u>Marilyn Moy</u> Marilyn Moy</p>
--

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following patents and printed publications are referred to in the body of the specification:

- U.S. Patent No. 4,683,195 issued 7/28/87 to Mullis *et al.*;
- U.S. Patent No. 4,683,202 issued 7/28/87 to Mullis;
- U.S. Patent No. 5,652,096 issued 7/29/97 to Cimino;
- U.S. Patent No. 5,608,039 issued 3/4/97 to Pastan *et al.*;
- U.S. Patent No. 4,016,043 issued 4/5/77 to Schuurs *et al.*;
- U.S. Patent No. 4,424,279 issued 1/3/84 to Bohn *et al.*;
- U.S. Patent No. 4,018,653 issued 4/19/77 to Mennen;

- Weiss *et al.*, "Signal transduction by lymphocyte antigen receptors," *Cell* 76:263-274 (1994);
- Cantrell, "T Cell Antigen Receptor Signal Transduction Pathways," *Annu. Rev. Immunol.*, 14:259-274 (1996);
- Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Biological Studies," *Proc. Natl. Acad. Sci. USA* 46:453 (1960);
- Doty *et al.*, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," *Proc. Natl. Acad. Sci. USA* 46:461 (1960);
- Wallace *et al.*, (1985) "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," *Biochimie* 67:755-762;
- Studencki and Wallace, "Allele-Specific Hybridization Using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Human β^A - and β^S -Globin Genes," *DNA* 3:7-15 (1984);
- Studencki *et al.*, (1985) "Discrimination Among the Human, β^A , β^S , and β^C -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," *Human Genetics* 37:42-51;
- Smith and Waterman, "Comparison of Biosequences," *Adv. Appl. Math.* 2:482-489 (1981);
- Needleman and Wunsch, "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," *J. Mol. Biol.* 48:443-453 (1970);
- Pearson and Lipman, "Improved Tools for Biological Sequence Comparison," *Proc. Natl. Acad. Sci. USA* 85:2444 (1988);
- Exley *et al.*, "Association of phosphatidylinositol-3-kinase with a specific sequence of the T cell receptor chain is dependent on T cell activation," *J. Biol. Chem.* 269:15140-15146 (1994);
- Cambier *et al.*, "Differential binding activity of ARH1/TAM motifs," *Immunol. Lett.* 44:77-80 (1995);

- Isakov *et al.*, "ZAP-70 binding specificity to T cell receptor tyrosine-based activation motifs: the tandem SH2 domains of ZAP-70 bind distinct tyrosine-based activation motifs with varying affinity," *J. Exp. Med.* 181:375-380 (1995);
- Osman *et al.*, "The protein interactions of the immunoglobulin receptor family tyrosine-based activation motifs present in the T cell receptor subunits and the CD3, δ and chains," *Eur. J. Immunol.* 26:1063-1068 (1996);
- Caplan *et al.*, "Cell-surface expressed T-cell antigen-receptor chain is associated with the cytoskeleton," *Proc. Natl. Acad. Sci. USA* 92:4768-4772 (1995);
- Rozdzial *et al.*, "Tyrosine-phosphorylated T cell receptor chain associates with actin cytoskeleton upon activation of mature T lymphocytes, *Immunity* 3:623-633 (1995);
- Bolen *et al.*, "Nonreceptor tyrosine protein kinases," *Oncogene* 8:2025-2031 (1993);
- Peri *et al.*, "Tyrosine protein kinases in T lymphocytes," *Chem. Immunol.* 59:19-39 (1994);
- Jayaraman *et al.*, "Regulation of the Inositol 1,4,5-trisphosphate receptor by tyrosine phosphorylation," *Science* 272:1492-1494 (1996);
- Cheng *et al.*, "Syk tyrosine kinase required for mouse viability and B-cell development," *Nature* 378:303-306 (1995);
- Fargnoli *et al.*, "Syk mutation in Jurkat E6-derived clones results in lack of p72syk expression," *J Biol. Chem.* 270:26533-26537 (1995);
- Turner *et al.*, "Perinatal lethality and blocked B-cell development in mice lacking the tyrosine kinase Syk," *Nature* 378:298-302 (1995);
- Arpaia *et al.*, "Defective T cell receptor signaling and CD8+ thymic selection in humans lacking ZAP-70 kinase," *Cell* 76:947-958 (1994);
- Chan *et al.*, "ZAP-70 deficiency in an autosomal recessive form of severe combined immunodeficiency," *Science* 264:1599-1601 (1994);
- Elder *et al.*, "Human severe combined immunodeficiency due to a defect in ZAP-70, a T cell tyrosine kinase," *Science* 264:1596-1599 (1994);

- Negishi *et al.*, "Essential role for ZAP-70 in both positive and negative selection of thymocytes," *Nature* 376:435-438 (1995);
- Chan *et al.*, "ZAP-70: a 70 kd protein-tyrosine kinase that associates with the TCR ζ chain," *Cell* 71:649-662 (1992);
- Watts *et al.*, "Identification by electrospray ionization mass spectrometry of the sites of tyrosine phosphorylation induced in activated Jurkat T cells on the protein tyrosine kinase ZAP-70," *J. Biol. Chem.* 269:29520-29529 (1994);
- Guanghai *et al.* "Distinct tyrosine phosphorylation sites within ZAP-70 mediate activation and negative regulation of antigen receptor function," *Mol. Cell. Biol.* (1996)¹
- Chan *et al.*, "Activation of ZAP-70 kinase activity by phosphorylation of tyrosine 493 is required for lymphocyte antigen receptor function," *EMBO J.* 14:2499-2508 (1995);
- Wange *et al.*, "Activating and inhibitory mutations in adjacent tyrosines in the kinase domain of ZAP-70," *J. Biol. Chem.* 270:18730-18733 (1995);
- Wange *et al.*, "Tandem SH2 domains of ZAP-70 bind to T cell antigen receptor and CD3 from activated Jurkat T cells," *J. Biol. Chem.* 268:19797-19801 (1993);
- Iwashima *et al.*, "Sequential interactions of the TCR with two distinct cytoplasmic tyrosine kinases," *Science* 263:1136-1139 (1994);
- Wange *et al.*, "F2(Pmp)2-TAM 3, a novel competitive inhibitor of the binding of ZAP-70 to the T cell antigen receptor, blocks early T cell signaling," *J. Biol. Chem.* 270:944-948 (1995);
- Qian *et al.*, "Dominant-negative Zeta-associated Protein 70 Inhibits T Cell Antigen Receptor Signaling," *J. Exp. Med.* 183:611-620 (1996);
- van Oers *et al.*, "Constitutive tyrosine phosphorylation of the T-cell receptor (TCR) subunit: regulation of TCR-associated protein tyrosine kinase activity by TCR ζ ," *Mol. Cell. Biol.* 13:5771-5780 (1993);

¹ Applicant is unable to locate and provide Examiner with a copy of this reference at this time.

- Wiest *et al.*, "TCR activation of ZAP-70 is impaired in CD4+CD8+ thymocytes as a consequence of intrathymic interactions that diminish available p56lck," *Immunity* 4:495-504 (1996);
- Desiderio *et al.*, "The Itk/Btk/Tec Family of Protein-Tyrosine Kinases," *Chem. Immunol.* 59:191-208 (1994);
- Liao *et al.*, "Altered T cell receptor signaling and disrupted T cell development in mice lacking Itk," *Immunity* 3:757-769 (1995);
- Gibson *et al.*, "The EMT/ITK/TSK (EMT) tyrosine kinase is activated during TCR signaling," *J. Immunol.* 156:2716-2722 (1996);
- Bustelo *et al.*, "Product of the Vav protooncogene defines a new class of tyrosine protein kinase substrates," *Nature* 356: 68-74 (1992);
- Donovan *et al.*, "The protein product of the c-cbl protooncogene is the 120-kDa tyrosine-phosphorylated protein in Jurkat cells activated via the T cell antigen receptor," *J. Biol. Chem.* 269:22921-22924 (1994);
- Jackman *et al.*, "Molecular cloning of SLP-76, a 76-kDa tyrosine phosphoprotein associated with Grb2 in T cells," *J. Biol. Chem.* 270:7029-7032 (1995);
- Harrison *et al.*, "Phosphorylation of human erythrocyte band 3 by endogenous p72syk," *J. Biol. Chem.* 269:955-959 (1994);
- Peters *et al.*, "Syk, activated by cross-linking the B-cell antigen receptor, localizes to the cytosol where it interacts with and phosphorylates alpha-tubulin on tyrosine," *J. Biol. Chem.* 271:4755-4762 (1996);
- Ley *et al.*, "Tyrosine phosphorylation of tubulin in human T lymphocytes," *Eur. J. Immunol.*, 24:99-106 (1994);
- Huby *et al.*, "Interactions between the Protein-tyrosine Kinase ZAP-70, the Proto-oncoprotein Vav, and Tubulin in Jurkat T Cells," *J. Biol. Chem.*, 270:30241-30244 (1995);
- Wardenburg *et al.*, "Phosphorylation of SLP-76 by the ZAP-70 protein tyrosine kinase is required for T cell receptor function," *J. Biol. Chem.*, In press (1996);
- Wu *et al.*, "Vav and SLP-76 interact and functionally cooperate in IL-2 gene activation," *Immunity* 4:593-602 (1996);

- Fusaki *et al.*, "Physical and functional interactions of protein tyrosine kinases, p59fyn and ZAP-70, in T cell signaling," *J. Immunol.* 156:1369-1377 (1996);
- Vogel *et al.*, "The SH3 domain of p56lck is involved in binding to phosphatidylinositol 3'-kinase from T lymphocytes," *Mol. Cell. Biol.*, 13:7408-7417 (1993);
- Thome *et al.*, "Syk and ZAP-70 mediate recruitment of p56lck/CD4 to the activated T cell receptor/CD3/ complex," *J. Exp. Med.*, 181:1997-2006 (1995);
- Hatada *et al.*, "Molecular basis for interaction of the protein tyrosine kinase ZAP-70 with the T-cell receptor," *Nature* 377:32-38 (1995);
- Shiue *et al.*, "Syk is activated by phosphotyrosine-containing peptides representing the tyrosine-based activation motifs of the high affinity receptor for IgE," *J. Biol. Chem.* 270:10498-10502 (1995);
- Neumeister *et al.*, "Binding of ZAP-70 to phosphorylated T-cell receptor and enhances its autophosphorylation and generates specific binding sites for SH2 domain-containing proteins," *Mol. Cell. Biol.* 15:3171-3178 (1995);
- Isakov *et al.*, "Purification and characterization of human ZAP-70 protein tyrosine kinase from a baculovirus expression system," *J. Biol. Chem.* 271:15753-15761 (1996);
- Katzav *et al.*, "The protein tyrosine kinase ZAP-70 can associate with the SH2 domain of proto-vav," *J. Biol. Chem.* 269:32579-32585 (1994);
- Fournel *et al.*, "Association of tyrosine protein kinase ZAP-70 with the protooncogene product p120c-cbl in T lymphocytes," *J. Exp. Med.* 183:301-306 (1996);
- Downward, "The GRB2/Sem-5 adaptor protein," *FEBS Lett.* 338: 113-117 (1994);
- Meisner *et al.*, "Interaction of Cbl with Grb2 and Phosphatidylinositol-3'-Kinase in Activated Jurkat Cells," *Mol. Cell. Biol.* 15:3571-3578 (1995);
- Holsinger *et al.*, "Signal transduction in T lymphocytes using a conditional allele of Sos," *Proc. Natl. Acad. Sci. USA* 92:9810-9814 (1995);

- Ravichandran *et al.*, "Interaction of Shc with Grb2 regulates association of Grb2 with mSOS," *Mol. Cell. Biol.* 15:593-600 (1995);
- Osman *et al.*, "A comparison of the interaction of Shc and the tyrosine kinase ZAP-70 with the T cell antigen receptor chain tyrosine-based activation motif," *J. Biol. Chem.* 270:13981-13986 (1995);
- Motto *et al.*, "In vivo association of Grb2 with pp116, a substrate of the T cell antigen receptor-activated protein tyrosine kinase," *J. Biol. Chem.* 269:21608-21613 (1994);
- Buday *et al.*, "A complex of Grb2 adaptor protein, Sos exchange factor, and a 36-kDa membrane-bound tyrosine phosphoprotein is implicated in ras activation in T cells," *J. Biol. Chem.* 269:9019-9023 (1994);
- Reif *et al.*, "SH3 domains of the adapter molecule Grb2 compete with two proteins in T cells: the guanine nucleotide exchange protein SOS and a 75-kDa protein that is a substrate for T cell antigen receptor-activated tyrosine kinases," *J. Biol. Chem.* 269:14081-14087 (1994)
- Fukazawa *et al.*, "T cell activation-dependent association between the p85 subunit of the phosphatidyl 3-kinase and Grb2/phospholipase C- γ 1-binding phosphotyrosyl protein," *J. Biol. Chem.* 270:36-38, 20177-20182 (1995);
- Liu *et al.*, "Activation-modulated association of 14-3-3 proteins with Cbl in T cells," *J. Biol. Chem.* 271:14591-14595 (1996);
- Reedquist *et al.*, "Stimulation through the T cell receptor induces Cbl association with Crk proteins and guanine nucleotide exchange protein C3G," *J. Biol. Chem.* 271:8435-8442 (1996);
- Motto *et al.*, "Implications of the GRB2-associated phosphoprotein SLP-76 in T cell receptor-mediated interleukin 2 production," *J. Exp. Med.* 183:1937-1943 (1996);
- McFarland *et al.*, "Protein tyrosine phosphatases involved in lymphocyte signal transduction," *Chem. Immunol.* 59:40-61 (1994);
- Plas *et al.*, "Direct regulation of ZAP-70 by SHP-1 in T cell antigen receptor signaling," *Science* 272:1173-1176 (1996);

- Kon-Kozlowski *et al.*, "The tyrosine phosphatase PTP1C associates with Vav, Grb2, and mSos1 in hematopoietic cells," *J. Biol. Chem.* 271:3856-3862 (1996);
- Marengere *et al.*, "Regulation of T cell receptor signaling by tyrosine phosphatase SYP association with CTLA-4," *Science* 272:1170-1173 (1996);
- Douillard and Hoffman, *Basic Facts about Lymphocyte Hybridomas*, in Compendium of Immunology Vol II, ed. by Schwartz, 1981;
- Kohler and Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," *Nature* 256: 495-497 (1975);
- Kohler and Milstein, "Derivation of specific antibody-producing tissue culture and tumor lines by cell fusion," *Euro. J. of Immunology* 6: 511-519 (1976);
- Reading, "Theory and Methods for Immunization in Culture and Monoclonal Antibody Production," *J. of Immuno. Meth.* 53: 261-291, 1982;
- Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 2d ed. (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.;
- *Current Protocols in Molecular Biology* (1996) John Wiley and Sons, Inc., N.Y.;
- Sinha *et al.*, "Polymer support oligonucleotide synthesis XVIII^(1,2): use of β -cyanoethyl-N,N-dialkylamino-/N-morpholino phosphoramidite of deoxynucleosides for the synthesis of DNA fragments simplifying deprotection and isolation of the final product," *Nuc. Acids Res.* 12:4539 (1984);
- Samelson *et al.*, "Association of the fyn protein-tyrosine kinase with the T-cell antigen receptor," *Proc. Natl. Acad. Sci. USA* 87:4358-4362 (1990);
- Kung *et al.*, "Monoclonal antibodies defining distinctive human T cell surface antigens," *Science* 206:347-349 (1979);
- Mizushima *et al.*, "pEF-BOS, a powerful mammalian expression vector," *Nuc. Acids Res.* 18:5322 (1990);
- Seed, "An LFA-3 cDNA encodes a phospholipid-linked membrane protein homologous to its receptor CD2," *Nature* 329:840-842 (1987);
- Nagata *et al.*, "Molecular cloning and expression of cDNA for human granulocyte colony-stimulating factor," *Nature* 319: 415-418 (1986);

- Uetsuki *et al.*, "Isolation and Characterization of the Human Chromosomal Gene for Polypeptide Chain Elongation Factor-1 α ," *J. Biol. Chem.*, 264:5791-5798 (1989);
- Spencer *et al.*, "Controlling signal transduction with synthetic ligands." *Science* 262:1019-1024 (1993);
- Berger *et al.*, "Secreted placental alkaline phosphatase: a powerful new quantitative indicator of gene expression in eukaryotic cells," *Gene* 66:1-10 (1988);
- Sloan-Lancaster *et al.*, "Regulation of ZAP-70 intracellular localization: visualization with the green fluorescent protein," *J. Exp. Med.* 186:1713-1724 (1997);
- GENBANK ACCESSION No. L05148;
- GENBANK ACCESSION No. Z29630;
- GENBANK ACCESSION No. M96995;
- GENBANK ACCESSION No.X16316;
- GENBANK ACCESSION No.X57110;
- Zhang *et al.*, "LAT: the ZAP-70 tyrosine kinase substrate that links T cell receptor to cellular activation," *Cell* 92:83-92 (1998);
- Songyang *et al.*, "Specific motifs recognized by the SH2 domains of Csk, 3BP2, fps/fes, GRB-2, HCP, SHC, Syk and Vav," *Mol. Cell. Biol.* 14:2777-2785 (1994);
- Alland *et al.*, "Dual myristylation and palmitoylation of Src family member p59^{lyn} affects subcellular localization," *J. Biol. Chem.* 269:16701-16705 (1994);
- Shenoy-Scaria *et al.*, "Cysteine of Src family protein tyrosine kinases determines palmitoylation and localization in caveolae" *J. Cell Biol.* 126:353-363 (1994);
- Simons and Ikonen, "Functional rafts in cell membranes" *Nature* 387:569-572 (1997);
- Brown and Rose, "Sorting of GPI-anchored proteins to glycolipid-enriched membrane subdomains during transport to the apical cell surface" *Cell* 68:533-544 (1992);

- Marth *et al.*, "Lymphocyte activation provokes modification of a lymphocyte-specific protein tyrosine kinase (p56lck)," *J. Immunol.* 142:2430-2437 (1989); and
- Clipstone and Crabtree, "Identification of calcineurin as a key signaling enzyme in T-lymphocyte activation" *Nature* 357:695-697 (1992).

Applicants have become aware of the following printed publications cited in a related foreign application:

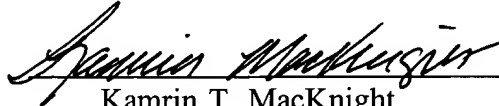
- GENBANK ACCESSION No. AA535611;
- Sieh *et al.*, "Grb2 and phospholipase C-gammal associate with a 36- to 38-kilodalton phosphotyrosine protein after T-cell receptor stimulation," *Mol. Cell. Biol.* 14:4435-42 (1994);
- Weber *et al.*, "Molecular cloning of the cDNA encoding pp36, a tyrosine-phosphorylated adapter protein selectively expressed by T cells and natural killer cells," *J. Exp. Med.* 187:1157-61 (1998); and
- Zhang *et al.*, "LAT: the ZAP-70 tyrosine kinase substrate that links T cell receptor to cellular activation," *Cell* 92:83-92 (1998).

Applicants has become aware of the following printed publication, copy attached, which may be material to the examination of the present Application. The Examiner is requested to make this publication of official record in this Application.

- Huang *et al.*, "Cloning and characterization of Lnk, a signal transduction protein that links T-cell receptor activation signal to phospholipase C γ_1 , Grb2, and phosphatidylinositol 3-kinase," *Proc. Natl. Acad. Sci. USA* 92:11618.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: May 25, 2001


Kamrin T. MacKnight
Registration No. 38,230

MEDLEN & CARROLL, LLP
220 Montgomery Street, Suite 2200
San Francisco, California 94104
415/705-8410